REMARKS

The Present Invention

The invention is drawn to a method of enhancing bone density or formation, an adenoviral vector, and a bone graft.

The Pending Claims

Upon entry of this amendment, claims 1-4, 6-12, 17-19, 21-23, 25, 29-33, 38-62 will be pending. Claims 1-4, 6-12, 17, 18, and 44-51 are directed to the method, claims 19, 21, 38-43, and 52-57 are directed to the adenoviral vector, and claims 22, 23, 25, 29-33, and 58-62 are directed to the bone graft.

Discussion of Claim Amendments

Claims 1, 19, and 22 have been amended to point out more particularly and claim more distinctly the present invention. Claims 1, 19, and 22 have been amended to incorporate a portion of the subject matter of claims 4, 5, 26-28, 36, and 37. New claims 44-62 are supported by the specification at, for example, page 2, line 34 – page 4, line 2, page 6, line 21 – page 8, line 3, and page 9, line 31 – page 10, line 14. Claims 5, 28, 36, and 37 have been canceled. Accordingly, no new matter has been added by way of these amendments.

The Office Action

The Office Action acknowledges that the rejection under Section 112, first paragraph, has been withdrawn in view of Applicants' previous amendment. Claims 1-3, 5, 6, 17-19, 21, 22, and 25 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by, or in the alternative, under 35 U.S.C. § 103(a) as being obvious over, WO 95/24473 (Hu et al.). Claims 1-3, 5, 6, 17-19, 21, 22, and 25 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by, or in the alternative, under 35 U.S.C. § 103(a) as being obvious over, U.S. Patent 5,935,820 (Hu et al.). Claims 1, 3, 6-8, 17, 18, 22, 23, 25, and 29 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent 6,398,816 (Breitbart et al.). Claims 1, 2, 6-8, 10, 17, and 18 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over the disclosures of U.S. Patent 6,525,030 (Eriksson) and U.S. Patent 6,475,480 (Mehtali et al.). Reconsideration of these rejections is hereby requested.

Discussion of Rejections Under 35 U.S.C. § 102

Claims 1-3, 5, 6, 17-19, 21, 22, and 25 have been rejected under Section 102(b) and 102(e) as allegedly being anticipated by, or in the alternative, under Section 103(a) as being obvious over, WO 95/24473 ("the '473 PCT application") and U.S. Patent 5,935,820 ("the '820 patent"), respectively. These rejections are respectfully traversed for the reasons set forth below.

The Office Action contends that both the '473 PCT application and the '820 patent disclose the use of a polynucleotide encoding VEGF2 to promote bone growth, which can be delivered via adenoviral delivery to cells either *ex vivo* or *in vivo*. Applicants note that claim 5 has been canceled. Claims 1, 19, and 22 have been amended to further define the vascular endothelial growth factor employed in the adenoviral vector. Neither the '473 PCT application nor the '820 patent discloses or suggests the use of any of the vascular endothelial growth factors recited in amended claims 1, 19, or 22. The '473 PCT application and the '820 patent also do not disclose or suggest any of the osteogenic proteins recited in claims 44, 52, and 58. Accordingly, neither the '473 PCT application nor the '820 patent anticipates or renders obvious the subject matter of claims 1, 19, 22, 44, 52, and 58, or claims depending therefrom.

Claims 1, 3, 6-8, 17, 18, 22, 23, 25, and 29 have been rejected under Section 102(e) as allegedly being anticipated by U.S. Patent 6,398,816 ("the '816 patent"). The '816 patent allegedly discloses using an adenoviral vector encoding one or more bioactive molecules (e.g., VEGF, BMPs, and PDGF) to transduce cells (e.g., periosteal cells), whereby the genetically engineered cells can be incorporated into a prosthesis for tissue (e.g., bone or cartilage) repair. The '816 patent, however, does not disclose or suggest an adenoviral vector encoding any of the VEGFs recited in amended claims 1, 19, and 22, or an adenoviral vector encoding any of the osteogenic proteins recited in new claims 44, 52, and 58. Moreover, in contrast to the Office Action's assertion, the '816 patent discloses the use of a nucleic acid encoding VEGF to treat *skin* or *wounds*, not to enhance bone density or formation, as required by the pending claims. For example, the '816 patent identifies VEGF as a "general growth factor important in wound healing" (see col. 6, lines 36-39) and distinguishes other bioactive molecules (e.g., BMPs) as bone growth factors (see col. 6, lines 33-34). Moreover, the '816 patent describes VEGF as aiding in healing, repair, or formation of skin (see col. 4, lines 54-57), which is disclosed as an alternative to the use of other factors for healing, repair, or formation of bone (see col. 4, lines 47-50). Thus, while the '816 patent does disclose the use of VEGF for healing skin, the '816 patent does not disclose or suggest the use of VEGF for promoting bone

growth. As such, the '816 patent does not anticipate or render obvious the subject matter of the pending claims.

Accordingly, because the pending claims define novel and unobvious subject matter in view of the '473 PCT application, the '820 patent, and the '816 patent, the Section 102 and 103 rejections based on these cited references should be withdrawn.

Discussion of Rejections Under 35 U.S.C. § 103

Claims 1, 2, 6-8, 10, 17, and 18 have been rejected under Section 103 as allegedly being unpatentable over the combined disclosures of U.S. Patent 6,525,030 ("the '030 patent") and U.S. Patent 6,475,480 ("the '480 patent"). This rejection is respectfully traversed for the reasons set forth below.

To establish a *prima facie* case of obviousness under Section 103 based on a combination of references, (i) the references must disclose or suggest every element of the claimed invention, (ii) there must be a motivation to combine the references, and (iii) the combination of references must provide a reasonable expectation of success for making the claimed invention. M.P.E.P. § 2143.

The '030 patent allegedly discloses a method for stimulating bone growth by delivering a gene that promotes bone growth to periosteal cells. The bone growth-promoting gene can be any of those listed in Table 3 of the '030 patent, such as VEGF, FGF, and TGF-beta. An aqueous solution of the gene is delivered to cells *in vivo* by microneedle injection. The '030 patent does not disclose the use of an adenoviral vector for gene delivery. Indeed, the specification of the '030 patent states that the disclosed gene delivery method "is useful for delivery of a suspension of genetic material alone, *without delivery of infectious viral material*" (see col.7, lines 47-49, emphasis added). The '030 patent also does not disclose or suggest an adenoviral vector encoding any of the VEGFs recited in amended claim 1 (and claims depending therefrom). The disclosure of the '480 patent allegedly cures the deficiencies in the '030 patent by allegedly disclosing an adenoviral vector encoding a gene of interest, which provides for improved gene expression in a mammal. The Office Action concludes that one of ordinary skill in the art would have been motivated to modify the disclosure of the '030 patent and employ an adenoviral vector as disclosed in the '480 patent to increase expression of the bone-growth promoting gene.

Applicants submit that one of ordinary skill in the art would not have been motivated to combine the disclosures of the '030 and '480 patents to arrive at the presently claimed invention. To do so, one of ordinary skill in the art would have to disregard the teachings of the '030 patent against the use of viral delivery of genetic material, and instead employ an

adenoviral vector (as disclosed in the '480 patent) to deliver a bone growth-promoting gene to cells. The Office Action has not provided any evidence for a motivation to combine the cited references in the precise manner required to result in the present invention.

Accordingly, the Office Action has failed to establish a *prima facie* case of obviousness, and the Section 103 rejection based on the '030 patent and the '480 patent should be withdrawn.

Conclusion

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent.

Respectfully submitted,

Heather Kissling, Reg. No. 45,790
LEYDIG, VOIT & MAYER, LTD.
Two Prudential Plaza, Suite 4900
180 North Stetson
Chicago, Illinois 60601-6780
(312) 616-5600 (telephone)
(312) 616-5700 (facsimile)

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